REMARKS/ARGUMENTS

Upon entry of this amendment, claims 42, 45-52, and 54 are pending in this application and are presented for examination. Claims 1-41, 43-44, 53, and 55-56 have been canceled without prejudice to future prosecution. Claims 42, 45-46, 48-49, and 54 have been amended.

Support for the amendments to the claims is found, for example, on page 5, lines 27-34; on page 6, lines 13-21; from page 18, line 36 to page 19, line 7; in Table 1 on page 51 (GRO3 and HNL); in Table 1 on page 55 (MMP-12 and elafin); and in Table 1 on page 56 (COL6A3) of the instant specification.

No new matter has been introduced with the foregoing amendments. Reconsideration is respectfully requested.

I. ELECTION/RESTRICTIONS

The Examiner has withdrawn claim 46 as allegedly being directed to a non-elected species (*see,* Office Action at page 2). Applicant has amended this claim to recite the originally elected species of the MMP-12 gene. As a result, Applicant believes that claim 46 should be included in the group of elected subject matter.

II. CLAIM OBJECTION

The Examiner has objected to claim 42 as allegedly missing an appropriate conjunction in between parts (d) and (e) of the claim (*see,* Office Action at page 18). In response, Applicant has amended claim 42 to include an "and" in between part (d) (now part (a)(iv)) and part (e) (now part (a)(v)) of the claim. Thus, Applicant respectfully requests withdrawal of the present claim objection.

III. REJECTION UNDER 35 U.S.C. § 112, SECOND PARAGRAPH

Claims 42, 45, 47-52, and 54 were rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite. To the extent the rejection applies to the amended claims, Applicant respectfully traverses the rejection.

A. Claim 42

The Examiner alleges that claim 42 recites alternative limitations in parts (a)-(e) of the claim and is unclear regarding whether an increase in the expression level of the MMP-12 gene is indicative of both a UC and a CD phenotype or either one of the phenotypes (*see,* Office Action at pages 4-5).

In order to expedite prosecution of the present case, Applicant has amended claim 42 to clarify that the claimed method comprises determining the expression level of *each* of the following genes in the test colon cell: GRO3, HNL, MMP-12, elafin, *and* COL6A3. Claim 42 has also been amended to clarify that an increase in the expression level of *each* of the GRO3, HNL, MMP-12, elafin, *and* COL6A3 genes in the test colon cell relative to the expression level of the same gene in the normal colon cell is associated with a UC phenotype, whereas an increase in the expression level of *each* of the MMP-12 *and* elafin genes in the test colon cell relative to the expression level of the same gene in the normal colon cell *and* a normal expression level of *each* of the GRO3, HNL, *and* COL6A3 genes is associated with a CD phenotype.

B. Claim 45

With regard to claim 45, the Examiner alleges that the phrase "distinguishing between a UC or CD phenotype in said test colon cell" is unclear (*see,* Office Action at page 5).

In order to expedite prosecution of the present case, Applicant has amended claim 45 to clarify that the claimed method distinguishes a UC phenotype from a CD phenotype in the test colon cell.

In view of the foregoing remarks, the claims are definite and claim the present invention with particularity. Accordingly, Applicant respectfully requests withdrawal of the rejection under 35 U.S.C. § 112, second paragraph.

IV. REJECTION UNDER 35 U.S.C. § 103(a)

As set forth in M.P.E.P. § 2141 (I), the Patent Office's policy is to follow *Graham v. John Deere Co. of Kansas City*, 383 U.S. 1 (1966), in the consideration and determination of

obviousness under 35 U.S.C. § 103. The four factual inquires enunciated in *Graham* for determining obviousness are as follows:

(A) Determining the scope and contents of the prior art;

(B) Ascertaining the differences between the prior art and the claims in issue;

(C) Resolving the level of ordinary skill in the pertinent art; and

(D) Evaluating evidence of secondary considerations.

Recently, the U.S. Supreme Court affirmed the holding of *Graham* regarding obviousness. *See, KSR Int'l Co. v. Teleflex Inc.*, 127 S.Ct. 1727 (2007).

To establish a *prima facie* case of obviousness, three basic criteria must be met: (1) there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings; (2) there must be a reasonable expectation of success; and (3) the prior art reference must teach or suggest all the claim limitations. *See,* M.P.E.P. § 2143.

A. Alexander *et al.* in view of Poulakkainen *et al.*

Claims 42, 45, 47-48, 50-52, and 54 were rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Alexander *et al.* (*Digestive Diseases and Sciences*, 41:660-669 (1996)) in view of Poulakkainen *et al.* (*Gastroenterology*, 114:A1064 (1998)). To the extent the rejection applies to the amended claims, Applicant respectfully traverses the rejection.

The Examiner alleges that it would have been *prima facie* obvious for one of skill in the art to use all of the known genes involved in IBD in an array to determine an IBD or pre-IBD phenotype based on the teachings of Alexander *et al.* and Poulakkainen *et al.* (*see,* Office Action at page 9). In response, Applicant asserts that the presently claimed invention is not obvious in view of the cited art for at least the following reason: the combination of references does not teach or suggest all the elements of the presently claimed invention.

Applicant submits that the primary reference cited by the Examiner does not teach or suggest the presently claimed method of determining whether a test colon cell has a UC or CD phenotype comprising determining the expression level of *each* of the following genes in the test colon cell: GRO3, HNL, MMP-12, elafin, *and* COL6A3. Rather, Alexander *et al.* discloses the

differential expression of the protooncogenes H-*ras*, c-*myc*, c-*fos*, c-*jun*, *junB*, N-*myc*, c-*abl*, and c-*yes* in colonic epithelial cells of IBD patients. In fact, the Examiner has acknowledged that Alexander *et al.* does not specifically teach any of the claimed genes (*see,* Office Action at page 8).

However, the Examiner alleges that the genes listed in Table 1 of the instant specification, which includes the five claimed genes, are well known for their role in IBD (*see, id*). Contrary to the Examiner's allegation, Applicant asserts that the Examiner has improperly characterized the sequences disclosed in Table 1 as being well known for their role in IBD. Although these sequences were known in the art, Applicant submits that the differential expression of genes such as COL6A3 was never appreciated to have a role in IBD until the advent of the present invention. In fact, the instant specification is the first to show that overexpression of GRO3, HNL, MMP-12, elafin, *and* COL6A3 in test colon cells relative to normal colon cells is associated with a UC phenotype, while overexpression of MMP-12 *and* elafin in test colon cells relative to normal colon cells in conjunction with normal GRO3, HNL, and COL6A3 expression is associated with a CD phenotype. As such, Applicant believes that the Examiner has impermissibly used an inventive feature of the claimed invention in making this obviousness rejection.

The secondary reference cited by the Examiner fails to supply the teaching that is clearly lacking in Alexander *et al.* In particular, Applicant asserts that Poulakkainen *et al.* is completely silent regarding the presently claimed method of determining whether a test colon cell has a UC or CD phenotype comprising determining the expression level of *each* of the five claimed genes in the test colon cell. Rather, this reference only describes the differential expression of MMP-10, MMP-13, MMP-12, and TIMP-3 in intestinal ulcerations.

Since neither of the references cited by the Examiner contemplates the presently claimed invention, it necessarily follows that the *combination* of these references fails to disclose or suggest all of the elements of the presently claimed invention. Importantly, these references, even when *combined*, lack any teaching or suggestion whatsoever regarding the claimed method of determining whether a test colon cell has a UC or CD phenotype comprising determining the

expression level of *each* of the five claimed genes in the test colon cell. At best, the *combined* disclosures of the cited references teaches the differential expression of *only one* of the five claimed genes, MMP-12. Accordingly, the *combined* disclosures of Alexander *et al.* and Poulakkainen *et al.* do not render the claimed method obvious. Therefore, the Examiner is respectfully requested to withdraw the present rejection under 35 U.S.C. § 103(a).

B. Dieckgraefe *et al.* in view of Puolakkainen *et al.*

Claims 42, 45, 47-52, and 54 were rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Dieckgraefe *et al.* (*Gastroenterology*, 114:A964-965 (1998)) in view of Puolakkainen *et al.* To the extent the rejection applies to the amended claims, Applicant respectfully traverses the rejection.

The Examiner alleges that it would have been *prima facie* obvious for one of skill in the art to use all of the known genes involved in IBD in an array to determine an IBD or pre-IBD phenotype based on the teachings of Dieckgraefe *et al.* and Poulakkainen *et al.* (*see,* Office Action at page 15). In response, Applicant asserts that the presently claimed invention is not obvious in view of the cited art for at least the following reason: the combination of references does not teach or suggest all the elements of the presently claimed invention.

Applicant submits that the primary reference cited by the Examiner does not teach or suggest the presently claimed method of determining whether a test colon cell has a UC or CD phenotype comprising determining the expression level of *each* of the following genes in the test colon cell: GRO3, HNL, MMP-12, elafin, *and* COL6A3. Rather, Dieckgraefe *et al.* discloses an oligonucleotide probe array that detected changes in the expression of different classes of genes in IBD specimens, but without reference to any particular genes in those classes. In fact, Dieckgraefe *et al.* does not specifically teach or suggest any of the genes set forth in the presently claimed method.

The secondary reference cited by the Examiner fails to supply the teaching that is clearly lacking in Dieckgraefe *et al.* As discussed above, Poulakkainen *et al.* describes the differential expression of MMP-10, MMP-13, MMP-12, and TIMP-3 in intestinal ulcerations, but is completely silent regarding the presently claimed method of determining whether a test

colon cell has a UC or CD phenotype comprising determining the expression level of *each* of the five claimed genes in the test colon cell.

Since neither of the references cited by the Examiner contemplates the presently claimed invention, it necessarily follows that the *combination* of these references fails to disclose or suggest all of the elements of the presently claimed invention. Importantly, these references, even when *combined*, lack any teaching or suggestion whatsoever regarding the claimed method of determining whether a test colon cell has a UC or CD phenotype comprising determining the expression level of *each* of the five claimed genes in the test colon cell. At best, the *combined* disclosures of the cited references teaches the differential expression of *only one* of the five claimed genes, MMP-12. Accordingly, the *combined* disclosures of Dieckgraefe *et al.* and Poulakkainen *et al.* do not render the claimed method obvious. Therefore, the Examiner is respectfully requested to withdraw the present rejection under 35 U.S.C. § 103(a).

C. Alexander *et al.* in view of Poulakkainen *et al.* and Dieckgraefe *et al.*

Claims 42, 45, 47-52, and 54 were rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Alexander *et al.* in view of Poulakkainen *et al.* and Dieckgraefe *et al.* To the extent the rejection applies to the amended claims, Applicant respectfully traverses the rejection.

The Examiner alleges that it would have been *prima facie* obvious for one of skill in the art to use probes having a specified length to detect the expression of genes based on the teachings of Alexander *et al.*, Poulakkainen *et al.*, and Dieckgraefe *et al.* (*see,* Office Action at page 17). In response, Applicant asserts that the presently claimed invention is not obvious in view of the cited art for at least the following reason: the combination of references does not teach or suggest all the elements of the presently claimed invention.

As discussed above, none of the references cited by the Examiner teaches or suggests the presently claimed method of determining whether a test colon cell has a UC or CD phenotype comprising determining the expression level of *each* of the following genes in the test colon cell: GRO3, HNL, MMP-12, elafin, *and* COL6A3. Since none of these references contemplates the presently claimed invention, it necessarily follows that the *combination* of these references fails to teach or suggest all of the elements of the presently claimed invention. In fact,

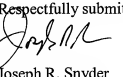
even when these references are *combined*, there remains a lack of any teaching or suggestion whatsoever regarding the presently claimed method of determining the expression level of *each* of the five claimed genes. At best, the *combined* disclosures of the cited references teaches the differential expression of *only one* of the five claimed genes, MMP-12. Accordingly, the *combined* disclosures of Alexander *et al.*, Poulakkainen *et al.*, and Dieckgraefe *et al.* do not render the claimed method obvious. In view of the foregoing remarks, the Examiner is respectfully requested to withdraw the present rejection under 35 U.S.C. § 103(a).

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 925-472-5000.

Respectfully submitted,



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